



DONALD G. VIDT, MD, EDITOR

# Atherosclerosis and hypertension: clues to effective prevention and treatment

## PRIMARY PREVENTION OF ATHEROSCLEROSIS

The proportion of sudden death to all deaths related to coronary heart disease remains unacceptably high and demands a concerted effort at the primary prevention of atherosclerosis. Hypertension is recognized as a major risk factor for atherosclerosis, and early detection and treatment of hypertension has been shown to reduce the total mortality from heart disease and the incidence of stroke. Paradoxically, clinical trials of antihypertensive drug therapies have achieved neither consistent nor dramatic results, perhaps representing a blunting of the expected benefit due to subtle effects of previously used antihypertensive drugs. New antihypertensive drugs, particularly calcium antagonists of the dihydropyridine class, may be more efficacious in preventing coronary heart disease by lowering blood pressure and by not causing adverse effects on lipids or other risk factors.

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## ANTIATHEROGENIC POTENTIAL OF ANTIHYPERTENSIVE DRUGS

Determining which of the available antihypertensive drugs has the best antiatherogenic potential in humans would be difficult, since the drugs affect not only blood pressure, but also cellular processes or metabolic pathways involved in the pathogenesis of

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atherosclerosis. For this reason, clinical trials are not likely to provide answers to this issue.

Clinical trials are fraught with problems such as great expense and questions about the validity of using death or presumed cardiac death as a clinical endpoint for atherosclerosis. Trials that assess growth of the atherosclerotic lesion may provide new insights into the effect of specific antihypertensive drugs on atherosclerosis. Although the techniques for quantitative lesion assessment are expensive and not as accurate as we might like, they may provide the most economical means of studying this problem.

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## CALCIUM ANTAGONISTS TO TREAT ATHEROSCLEROSIS

Clinical studies of calcium antagonists may identify effective treatment regimens to slow or prevent the long-term progression of atherosclerosis. Neither nifedipine nor nifedipine has been shown to prohibit progression of established coronary lesions, but nifedipine has been shown to exert a significant protective effect against the development of new lesions in patients with mild to moderate coronary artery disease. The Multicenter Isradipine Diuretic Atherosclerotic Study is evaluating the efficacy of isradipine compared with hydrochlorothiazide to retard the rate of progression of atherosclerotic lesions in the carotid arteries of hypertensive patients, using B-mode ultrasound to evaluate lesions.

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## MANAGING THE HYPERTENSIVE PATIENT WITH MULTIPLE RISK FACTORS

**H**ypertension, left ventricular hypertrophy, smoking, aging, obesity, and abnormalities in cholesterol, glucose, and insulin metabolism are all risk factors for major cardiovascular events such as stroke and myocardial infarction. The optimal treatment for hypertension would consider the entire range of risk factors in coronary heart disease. Such an agent has yet to be developed, but clinicians can make the most of currently available antihypertensive agents by considering not only a drug's ability to lower blood pressure to normotensive levels, but also its effects on such metabolic factors as serum lipoproteins and carbohydrate tolerance. When indicated, antihypertensive therapy should be supplemented with active lipid-lowering therapies.

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## ARTERIAL RESPONSES TO HYPERTENSION

**H**ypertension causes major changes in the arterial wall. In the medial layer, hypertension causes a prominent increase in cellular mass, typically involving smooth muscle cell (SMC) hypertrophy and sometimes polyploidy, in addition to an increase in collagen and elastin. Cell culture studies have indicated that SMC growth can be stimulated by a variety of vasoactive agents including catecholamines and angiotensin II.

In experiments with the Watanabe familial hyperlipidemic rabbit which develops hypercholesterolemia because of a defect in the LDL receptor, antihypertensive drugs such as propranolol, nifedipine, and verapamil have failed to arrest atherogenesis. However, the angiotensin-converting enzyme inhibitor captopril has inhibited atherogenesis and significantly reduced the cellularity of atherosclerotic lesions, suggesting that the drug may involve an action on cellular growth.

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